STN Search History

```
L1    QUE PRION
s l1 (s) (ligand) or (prion (s) binding (s) peptide)
L2    QUE L1 (S) (LIGAND) OR (PRION (S) BINDING (S) PEPTIDE)
 d rank
F1          861   DGENE
F2           85   BIOSIS
F3           85   SCISEARCH
F4           85   USPATFULL
F5           83   MEDLINE
F6           66   EMBASE
F7           59   CAPLUS
F8           56   ESBIOBASE
F9           48   LIFESCI
F10          43   WPIDS
F11          43   WPINDEX
F12          41   BIOTECHNO
F13          16   TOXCENTER
F14          15   BIOTECHABS
F15          15   BIOTECHDS
F16          15*  FEDRIP
F17          14   CANCERLIT
F18          14   PROMT
F19          12   CABA
F20          11   NLDB
F21           9   IFIPAT
F22           8   FSTA
F23           8   JICST-EPLUS
F24           6   EMBAL
F25           6   PASCAL
F26           4   AGRICOLA
F27           4   CIN
F28           3   PHIN
F29           2   BIOCOMMERCE
F30           2   DRUGNL
F31           2   DRUGUPDATES
F32           2   USPAT2
F33           1   CONFSCI
F34           1   DDFU
F35           1   DRUGU
F36           1   FROSTI
F37           1   PHAR
F38           1   IPA
     (FILE 'DGENE, BIOSIS, SCISEARCH, MEDLINE, EMBASE, CAPLUS, ESBIOBASE,
     LIFESCI, BIOTECHNO, TOXCENTER' ENTERED AT 09:20:15 ON 07 AUG 2002)
L3         30408 S PRION
L4           886 S L3 (S) (LIGAND OR (BINDING (5N) PEPTIDE))
L5           665 DUP REM L4 (221 DUPLICATES REMOVED)
L6             9 S L3 (S) (BINDING (5N) POLYPEPTIDE)
L7           665 S L5 NOT STEPTAVIDIN
L8             0 S L5 AND (NONAPEPTIDE OR ((TWENTY OR 20) (S) AMINO))
L9            22 S L7 AND ((LIGAND OR BIND###) (P) (METAL OR COPPER))

L10          643 L7 NOT L9
L11            7 L10 AND (LIGAND OR PEPTIDE OR POLYPEPTIDE) (S) (COMPLEX (10N)
                 (PRION OR PRP))
```

L6 ANSWER 1 OF 9 DGENE (C) 2002 THOMSON DERWENT

TI New polypeptides comprising prion protein sequences - useful for diagnosis or treatment of prion diseases e.g. Scrapie, BSE and Creutzfeldt-Jacob disease

IN Korth C; Moser M; Oesch B

AN AAW93571 protein DGENE

AB This invention describes a synthetic polypeptide comprising at least one "defined" PrP (**prion** protein) sequence or sequences derived therefrom that are recognised by a disease specific isoform of PrP, e.g. PrP(Sc), **binding** substances. The new **prion** protein **polypeptides** are useful in vaccines and pharmaceuticals for treatment of, and as diagnostic agents for diagnosis of Scrapie, BSE, Kuru and Creutzfeldt-Jacob disease. The polypeptides are also useful in pharmaceutical or chemical libraries for detection of PrP(Sc)-specific agents.

L6 ANSWER 1 OF 9 DGENE (C) 2002 THOMSON DERWENT
AN AAW93571 protein DGENE
TI New polypeptides comprising prion protein sequences - useful for diagnosis or treatment of prion diseases e.g. Scrapie, BSE and Creutzfeldt-Jacob disease
IN Korth C; Moser M; Oesch B
PA (PRIO-N) PRIONICS AG.
PI DE 19741607 A1 19990325 12p
AI DE 1997-19741607 19970920
PRAI DE 1997-19741607 19970920
DT Patent
LA German
OS 1999-205964 [18]

L6 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Association of scrapie prion protein and prion protein-RNA stem-loop with nuclear carbohydrate-binding protein 35 and other RNA-binding proteins.
AU Schroeder, Heinz C. (1); Scheffer, Ute; Forrest, Jock M. S.; Seve, Annie-Pierre; Rytik, Peter G.; Mueller, Werner E. G.
SO Neurodegeneration, (1994) Vol. 3, No. 3, pp. 177-189.
ISSN: 1055-8330.
AB A number of cellular proteins were identified that bind to the predicted RNA stem-loop structure of **prion** protein (PrP) RNA; a virtually identical set of RNA-binding proteins was found to associate with the trans-activating region TAR of the human immunodeficiency virus-1. The predicted hairpin elements of the PrP mRNA contain, like TAR RNA, a CUGGG sequence in the loop and a uridine- and adenine bulge in the stem; these features are unique among cellular RNAs. UV cross-linking of RNA-protein complexes formed between PrP RNA and HeLa nuclear protein yielded four prominent RNase-resistant complexes, in addition to some minor bands, which migrated at apprxeq 90, 68, 42, and 37-kDa under denaturing conditions. The presence of multiple PrP RNA-binding, as well as TAR RNA-**binding polypeptides** was also demonstrated in Northwestern assays with nuclear extracts from mouse ascites, liver, and spleen, whereas only one PrP RNA-binding protein (a doublet with an approximate molecular mass of 35 kDa) was found in brain extract from rat. The nuclear beta-galactoside-specific lectin, CBP35 (carbohydrate-binding protein with a molecular mass of 35 kDa), which has been identified in nuclear ribonucleoprotein (RNP) complexes from a variety of mammalian tissues and cells, was among those proteins which bind to PrP RNA. The cellular **prion** protein, PrP-c, was found to be unable to bind PrP RNA directly; however, this protein could be detected in the RNP/CBP35 complex formed between PrP RNA and rat brain extracts. Association of PrP-c with RNP/CBP35 complex was abolished by RNase treatment. CBP35 could be also detected in purified infectious scrapie **prions**, suggesting a possible role in **prion** replicatio

L9 ANSWER 3 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI **Copper binding** to octarepeat **peptides** of the **prion** protein monitored by mass spectrometry.
AU Whittal, Randy M.; Ball, Haydn L.; Cohen, Fred E.; Burlingame, Alma L.; Prusiner, Stanley B.; Baldwin, Michael A. (1)
SO Protein Science, (Feb., 2000) Vol. 9, No. 2, pp. 332-343.
ISSN: 0961-8368.
AB Electrospray ionization mass spectrometry (ESI-MS) was used to measure the **binding** of Cu2+ ions to synthetic **peptides** corresponding to sections of the sequence of the mature **prion** protein (PrP). ESI-MS demonstrates that Cu2+ is unique among divalent **metal** ions in **binding** to PrP and defines the location of the major Cu2+ **binding** site as the octarepeat region in the N-terminal domain, containing multiple copies of the repeat ProHisGlyGlyGlyTrpGlyGln. The stoichiometries of the complexes measured directly by ESI-MS are pH dependent: a peptide containing four octarepeats chelates two Cu2+ ions at pH 6 but four at pH 7.4. At the higher pH, the **binding** of multiple Cu2+ ions occurs with a high degree of cooperatively for peptides C-terminally extended to incorporate a fifth histidine. Dissociation constants for each Cu2+ ion **binding** to the octarepeat **peptides**, reported here for the first time, are mostly in the low micromolar range; for the addition of the third and fourth Cu2+ ions to the extended peptides at pH 7.4, KD's are <100 nM. N-terminal acetylation of the peptides caused some reduction in the stoichiometry of **binding** at both pH's. Cu2+ also **binds** to a peptide corresponding to the extreme N-terminus of PrP that precedes the octarepeats, arguing that this region of the sequence may also make a contribution to the Cu2+ complexation. Although the structure of the four-octarepeat peptide is not affected by pH changes in the absence of Cu2+, as judged by circular dichroism, Cu2+ **binding** induces a modest change at pH 6 and a major structural perturbation at pH 7.4. It is possible that PrP functions as a Cu2+ transporter by **binding** Cu2+ ions from the extracellular medium under physiologic and then releasing some or all of this **metal** upon exposure to acidic pH in endosomes or secondary lysosomes.

L9 ANSWER 4 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Studies on the **binding** of tandem octarepeat **prion** **peptides** to **metal** chelates using immobilized **metal** affinity chromatography.
AU MacKenzie, James (1); McCartney, Melissa (1); Boulis, Yannick (1); Vijayalakshmi, M. A.; Srikrishnan, Thamarapu (1)
SO Biophysical Journal., (Jan., 2000) Vol. 78, No. 1 Part 2, pp. 13A.
Meeting Info.: 44th Annual Meeting of the Biophysical Society. New Orleans, Louisiana, USA February 12-16, 2000
ISSN: 0006-3495.

L9 ANSWER 5 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Characterization and polyanion-binding properties of purified recombinant prion protein.
AU Brimacombe, Debbie B.; Bennett, Alan D. (1); Wusteman, Fred S.; Gill, Andrew C.; Dann, Janine C.; Bostock, Christopher J.
SO Biochemical Journal, (Sept. 15, 1999) Vol. 342, No. 3, pp. 605-613.
ISSN: 0264-6021.
AB Certain polysulphated polyanions have been shown to have prophylactic effects on the progression of transmissible spongiform encephalopathy disease, presumably because they **bind** to **prion** protein (PrP). Until now, the difficulty of obtaining large quantities of native PrP has precluded detailed studies of these interactions. We have over-expressed murine recombinant PrP (recPrP), lacking its

glycophosphoinositol membrane anchor, in modified mammalian cells. Milligram quantities of secreted, soluble and partially glycosylated protein were purified under non-denaturing conditions and the identities of mature-length aglycosyl recPrP and two cleavage fragments were determined by electrospray MS. **Binding** was assessed by surface plasmon resonance techniques using both direct and competitive **ligand-binding** approaches. recPrP **binding** to immobilized polyanions was enhanced by divalent **metal** ions. Polyanion **binding** was strong and showed complex association and dissociation kinetics that were consistent with **ligand**-directed recPrP aggregation. The differences in the **binding** strengths of recPrP to pentosan polysulphate and to other sulphated polyanions were found to parallel their in vivo anti-scrapie and in vitro anti-scrapie-specific PrP formation potencies. When recPrP was immobilized by capture on **metal**-ion chelates it was found, contrary to expectation, that the addition of polyanions promoted the dissociation of the protein.

L9 ANSWER 6 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI **Copper binding** to the prion protein: Structural implications of four identical cooperative **binding** sites.
AU Viles, John H.; Cohen, Fred E.; Prusiner, Stanley B.; Goodin, David B.; Wright, Peter E. (1); Dyson, H. Jane (1)
SO Proceedings of the National Academy of Sciences of the United States of America, (March 2, 1999) Vol. 96, No. 5, pp. 2042-2047. ISSN: 0027-8424.
AB Evidence is growing to support a functional role for the **prion** protein (PrP) in **copper** metabolism. **Copper** ions appear to **bind** to the protein in a highly conserved octapeptide repeat region (sequence PHGGGWGQ) near the N terminus. To delineate the site and mode of **binding** of Cu(II) to the PrP, the **copper**-**binding** properties of **peptides** of varying lengths corresponding to 2-, 3-, and 4-octarepeat sequences have been probed by using various spectroscopic techniques. A two-octarepeat peptide **binds** a single Cu(II) ion with Kd apprxeq 6 muM whereas a four-octarepeat peptide cooperatively **binds** four Cu(II) ions. Circular dichroism spectra indicate a distinctive structuring of the octarepeat region on Cu(II) **binding**. Visible absorption, visible circular dichroism, and electron spin resonance spectra suggest that the coordination sphere of the **copper** is identical for 2, 3, or 4 octarepeats, consisting of a square-planar geometry with three nitrogen **ligands** and one oxygen **ligand**. Consistent with the pH dependence of Cu(II) **binding**, proton NMR spectroscopy indicates that the histidine residues in each octarepeat are coordinated to the Cu(II) ion. Our working model for the structure of the complex shows the histidine residues in successive octarepeats bridged between two **copper** ions, with both the Nepsilon2 and Ndeltal imidazole nitrogen of each histidine residue coordinated and the remaining coordination sites occupied by a backbone amide nitrogen and a water molecule. This arrangement accounts for the cooperative nature of complex formation and for the apparent evolutionary requirement for four octarepeats in the PrP.

L9 ANSWER 8 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Prion protein selectively **binds copper**(II) ions.
AU Stockel, Johannes; Safar, Jiri; Wallace, Andrew C.; Cohen, Fred E.; Prusiner, Stanley B. (1)
SO Biochemistry, (May 19, 1998) Vol. 37, No. 20, pp. 7185-7193. ISSN: 0006-2960.
AB The infectious isoform of the **prion** protein (PrPSc) is derived from cellular PrP (PrPC) in a conversion reaction involving a dramatic

reorganization of secondary and tertiary structure. While our understanding of the pathogenic role of PrPSc has grown, the normal physiologic function of PrPC still remains unclear. Using recombinant Syrian hamster **prion** protein (SHaPrP(29-231)), we investigated **metal** ions as possible **ligands** of PrP. Near-UV circular dichroism spectroscopy (CD) indicates that the conformation of SHaPrP(29-231) resembles PrPC purified from hamster brain. Here we demonstrate by CD and tryptophan (Trp) fluorescence spectroscopy that **copper** induces changes to the tertiary structure of SHaPrP(29-231). **Binding** of **copper** quenches the Trp fluorescence emission significantly, shifts the emission spectrum to shorter wavelengths, and also induces changes in the near-UV CD spectrum of SHaPrP(29-231). The **binding** sites are highly specific for Cu2+, as indicated by the lack of a change in Tip fluorescence emission with Ca2+, Co2+, Mg2+, Mn2+, Ni2+, and Zn2+. **Binding** of Cu2+ also promotes the conformational shift from a predominantly alpha-helical to a beta-sheet structure. Equilibrium dialysis experiments indicate a **binding** stoichiometry of apprx2 **copper** molecules per PrP molecule at physiologically relevant concentrations, and pH titration of Cu2+ **binding** suggests a role for histidine as a chelating **ligand**. NMR spectroscopy has recently demonstrated that the octarepeats (PHGGGWGQ) in SHaPrP(29-231) lack secondary or tertiary structure in the absence of Cu2+. Our results suggest that each Cu2+ **binds** to a structure defined by two octarepeats (PHGGGWGQ) with one histidine and perhaps one glycine carbonyl chelating the ion. We propose that the **binding** of two **copper** ions to four octarepeats induces a more defined structure to this region

L9 ANSWER 9 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI SPONTANEOUS CONVERSION OF PRP-C TO PRP-S-C.
AU SULKOWSKI E
SO FEBS (FED EUR BIOCHEM SOC) LETT, (1992) 307 (2), 129-130.
CODEN: FEBLAL. ISSN: 0014-5793.
AB Octa-repeats of **prion** proteins (PrP) contain histidine and tryptophan residues which are known to function as **ligands** for transition **metals**. It is proposed that the spontaneous conversion of the PrPc (cellular) isoform into PrPSc (scrapie) isoform may be triggered by the coordination of these **metals**.

L9 ANSWER 16 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
TI **Binding** of **prion** octarepeat **peptide** to **metal** chelates.
AU Balakrishnan R.; Parashurama P.; Vijayalakshmi M.A.; Parthasarathy R.
SO International Journal of Bio-Chromatography, (1998) 4/1 (27-34).
Refs: 25
ISSN: 1068-0659 CODEN: IJOBEQ
AB A synthetic **prion** octarepeat peptide, PHGGGWGQ, **binds** with a decreasing avidity, to immobilized (agarose) chelates of transition **metals**: IDA-Cu(II) > IDA-Ni(II) > IDA-Zn(II). The residence time of the peptide on IDA-Ni(II) and IDA-Zn(II) columns is extended when Ca2+ ions are present in the mobile phase. Our findings document, in vitro, the complexation between the **metal** chelates, IDA-M(II), and the **prion** octarepeat peptide. One can envisage a transfer, in vivo, of the transition **metal** ions from their complexes with physiological carriers (amino acids, peptides), by a **ligand** exchange, to the tandem octarepeats (PHGGGWGQ)(n), of the **prions**.

L9 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2002 ACS
TI **Copper binding** to the N-terminal tandem repeat region of mammalian and avian prion protein: structural studies using synthetic peptides

AU Hornshaw, M. P.; McDermott, J. R.; Candy, J. M.; Lakey, J. H.
SO Biochem. Biophys. Res. Commun. (1995), 214(3), 993-9
CODEN: BBRCA9; ISSN: 0006-291X
AB Using CD spectroscopy we have investigated the effect of Cu2+ on the secondary structure of synthetic peptides Octa4 and Hexa4 corresponding to tetra-repeats of the octapeptide of mammalian PrP and the hexapeptide of chicken PrP. In addn., fluorescence spectroscopy was used to est. the dissocn. consts. (Kd), of Cu2+ binding by both peptides. Both peptides exhibited unusual CD spectra, complicated by the high proportion of arom. residues, revealing little secondary structure in aq. soln. Addn. of Cu2+ to Hexa4 induced an increase in random coil to resemble Octa4. The fluorescence of both peptides was quenched by Cu2+ and this was used to calc. Kd's of 6.7 .mu.M for Octa4 and 4.5 .mu.M for Hexa4. Other divalent cations showed lesser effects on the fluorescence of the peptides.

L9 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2002 ACS
TI **Copper binding** to the N-terminal tandem repeat regions of mammalian and avian prion protein
AU Hornshaw, M. P.; McDermott, J. R.; Candy, J. M.
SO Biochemical and Biophysical Research Communications (1995), 207(2), 621-9
CODEN: BBRCA9; ISSN: 0006-291X
AB Mammalian prion protein (PrP) is a normal cellular protein (PrPc) which through post-translational modification produces the infectious prion protein (PrPsc). We have shown, using mass spectrometry, that synthetic peptides contg. three or four copies of an octapeptide repeat sequence (PHGGGWGQ), found in highly conserved N-terminal domain of PrP, preferentially **bind copper** over other **metals**. Peptides from the analogous region of chicken PrP, which contains an N-terminal repeat domain of the hexapeptide (NPGYPH), showed similar specificity for **copper binding**. In addn., gel filtration chromatog. demonstrated concn. dependent **binding** of **copper** to the mammalian tetra repeat PrP peptide. These results suggest that PrP may be a **copper binding** protein in vivo.

L11 ANSWER 1 OF 7 DGENE (C) 2002 THOMSON DERWENT
AN AAW00326 peptide DGENE
TI New prion protein binding protein and its fragments - for diagnosis of spongiform encephalopathies and in drug screening, also immunogenic complexes, antisera and monoclonal antibodies
IN Brentani R R; De Souza S J; Martins V R
PA (LUDW-N) LUDWIG INST CANCER RES.
PI WO 9632128 A1 19961017 27p
AI WO 1996-US5028 19960411
PRAI US 1995-421059 19950412
DT Patent
LA English
OS 1996-476841 [47]
AN AAW00326 peptide DGENE
AB AAW00326 is a synthetic **prion** protein-**binding** **peptide**, it is a fragment of an isolated protein which has a molecular weight of 55-72 kD, by SDS-PAGE. The **peptide** is used to raise an antiserum which is used to identify nerve cells that present an anti-PrP (**prion** protein) protein on the surface and to detect the anti-**PrP** protein by **complex** formation. The **peptide** itself may similarly be used to detect **PrP**. The **peptide**, antibodies and antisera produced are useful in the diagnosis of PrP-associated diseases, especially Creutzfeldt-Jakob disease (CJD), scrapie and bovine spongiform encephalopathy (BSE). The **peptide** may also be used to screen potential drugs for the treatment of CJD, scrapie or BSE.